

(Applied Biosystems). From the 53 clones previously selected, several clones were found to encode the same amino acid sequence. Taking these degeneracies into account, four sequences of Affibody molecules expressed by clones selected in the ELISA binding assay are given in Figure 1 (Z<sub>HER2</sub> A-D). and identified in the sequence listing as SEQ ID NO: 2-5.

Please replace the paragraph bridging page 35, line 26, to

page 36, line <sup>7</sup>15, with the following amended paragraph:

Change(s) applied  
to document,

/K.P./

6/23/2011

A Biacore<sup>®</sup> 2000 instrument (Biacore AB) was used for real-time biospecific interaction analysis (BIA). A recombinant extracellular domain of HER2 (HER2-ECD), diluted in 10 mM NaAc, pH 4.5, was immobilized (about 2200 RU) on the carboxylated dextran layer of one flow-cell surface of a CM5 sensor chip (research grade) (BR-1000-14, Biacore AB) by amine coupling according to the manufacturer's instructions. Another flow-cell surface was activated and deactivated, to serve as a reference surface. For the Z<sub>HER2</sub> sample, the buffer was changed to HBS (5 mM HEPES, 150 mM NaCl, 3.4mM EDTA, 0.005% surfactant P20, pH 7.4) be gel filtration using a NAP<sup>™</sup>-10 column, ~~according to the manufacturer's protocol~~ according to the manufacturer's protocol (Amersham Biosciences), and the sample was thereafter filtrated

life of the SPA domain related HER2 binding moiety in isolation (this principle has been described ~~e-g~~ e.g., in WO91/01743).

Change(s) applied Please replace the paragraph bridging page 11, line <sup>36</sup>~~18~~, to  
to document page 12, line 20, with the following amended paragraph:

/K.P./

6/23/2011

Other options for the second and further moiety or moieties of a fusion polypeptide according to the invention include a moiety or moieties for therapeutic applications. In therapeutic applications, other molecules may also be coupled, covalently or non-covalently, to the inventive polypeptide by other means. Non-limiting examples include enzymes for "ADEPT" (antibody-directed enzyme prodrug therapy) applications using the polypeptide according to the invention for direction of the effector enzyme (~~e-g~~ e.g., carboxypeptidase); proteins for recruitment of effector cells and other components of the immune system; cytokines, such as IL-2, IL-12, TNF $\alpha$ , IP-10; procoagulant factors, such as tissue factor, von Willebrand factor; toxins, such as ricin A, Pseudomonas exotoxin, calceamicin, maytansinoid; toxic small molecules, such as auristatin analogs, doxorubicin. Also, the above named additional amino acids (notably hexahistidine tag, cysteine), provided with the aim of coupling chelators for radiosotopes to the polypeptide sequence,

Change(s) applied Please replace the paragraph bridging page 7, line <sup>27</sup>~~32~~  
to document, through page 8, line 12, with the following amended paragraph:

/K.P./

6/23/2011

"Binding affinity for HER2" refers to a property of a polypeptide which may be tested ~~e-g~~ e.g., by the use of surface Plasmon resonance technology, such as in Biacore<sup>®</sup> instrument. HER2 binding affinity may be tested in an experiment wherein HER2 is immobilized on a sensor chip of the instrument, and a sample containing the polypeptide to be tested is passed over the chip. Alternatively, the polypeptide to be tested is immobilized on a sensor chip of the instrument, and a sample containing HER2 is passed over the chip. The skilled person may then interpret the sensorgrams obtained to establish at least a qualitative measure of the polypeptide's binding affinity for HER2. If a quantitative measure is sought, ~~e-g~~ e.g., with the purpose to establish a certain  $K_D$  value for the interaction, it is again possible to use surface plasmon resonance methods. Binding values may ~~e-g~~ e.g., be defined in a Biacore<sup>®</sup> 2000 instrument (Biacore AB). HER2 is immobilized on a sensor chip of the instrument, and samples of the polypeptide whose affinity is to be determined are prepared by serial dilution and injected in random order.  $K_D$  values may then be calculated from the results, using ~~e-g~~ e.g., the 1:1 Langmuir binding model of the